**CONGENITAL MUSCULAR DYSTROPHIES**

Congenital muscular dystrophies (CMD) are a heterogeneous group of diseases including Walker Warburg Syndrome (WWS), Muscle-Eye-Brain Disease (MEB), Fukuyama Congenital Muscular Dystrophy (FCMD) and Congenital Muscular Dystrophy Type 1C (MDC1C). They usually present at birth or within the first 6 months of life. Initial signs include hypotonia, muscle weakness and the variable appearance of contractures.

WWS, MEB, FCMD and MDC1C are caused by mutations affecting glycosylation enzymes, proteins that add sugars to other proteins. In these diseases, defects in the sugar-adding mechanism disrupt the properties of α-dystroglycan, a protein critical for normal muscle function.

**GENETICS**

CMDs are autosomal recessively inherited neuromuscular disorders. An individual is affected if s/he receives two copies of a defective gene, one from each parent. Any person with one copy of the defective gene is a carrier; carriers do not have and will never develop the disease. Two carriers have a 25% chance that their child will be born with the condition.

**WHO SHOULD BE TESTED?**

- Individuals clinically suspected of being affected with WWS, MEB, FCMD, or MDC1C
- Individuals with a family history of WWS, MEB, FCMD or MDC1C, to determine carrier status
- Pregnancies at increased risk of being affected with WWS, MEB, FCMD or MDC1C

**TEST METHODS**

- Complete sequencing of the coding region and flanking exon/intron boundaries of the POMT1, POMT2, POMGnT1, FCMD and FKRP genes, to identify point mutations.

**POTENTIAL OUTCOMES & INTERPRETATION OF TEST RESULTS**

<table>
<thead>
<tr>
<th>Reason for referral</th>
<th>Gene Mutations Allele 1 / allele 2</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>None detected / none detected</td>
<td>This result does not support a diagnosis</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Mutation detected / none detected</td>
<td>This result is unable to confirm a diagnosis</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Mutation detected / mutation detected</td>
<td>This result confirms a diagnosis</td>
</tr>
<tr>
<td>Carrier testing</td>
<td>None detected / none detected</td>
<td>This individual is unlikely to be a carrier</td>
</tr>
<tr>
<td>Carrier testing</td>
<td>Mutation detected / none detected</td>
<td>This individual is a carrier and may transmit a mutation to offspring</td>
</tr>
</tbody>
</table>

For More Information

- **MEB** #253280
- **CMD1C** #606612
- **WWS** #236670
- **FCMD** #253800


To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-acgc.ca or the National Society of Genetic Counsellors website at www.nsgc.org

1. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the possibility that the individual carries a rare mutation not detected by this assay.

2. Additional testing such as muscle biopsy and serum creatine kinase analysis is strongly recommended, as it can be a useful complement to molecular testing.

3. The clinical course or severity of symptoms cannot be predicted by molecular analysis.

4. Test results should be interpreted in the context of clinical findings, family history, ethnic background and other laboratory data.

5. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.

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